Organic reactions in ionic liquids: a novel method for the synthesis of 2-arylthiobenzothiazoles by the S-arylation of benzolthiazole-2-thiol with diaryliodonium salts

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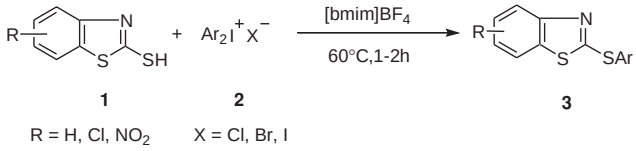
2-Arylthiobenzothiazoles were readily prepared in good yields by the S-arylation of benzothiazole-2-thiol with diaryliodonium salts at room-temperature in the ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4). The ionic liquid can be recycled and reused.

Keywords: ionic liquid, benzothiazole-2-thiol, diaryliodonium salts, 2-arylthiobenzothiazoles.

Room temperature ionic liquids, especially those based upon the 1-*n*-alkyl-3-methylimidazolium cation, have attracted growing interest in the last few years.[1] They offer an alternative and ecologically sound medium compared to conventional organic solvents, as they are non-volatile, recyclable, thermally robust, and show excellent solubility in a wide range of organic and inorganic materials. These media have been applied to non-catalytic[1,2] and catalytic reactions[1] as well as to selective extraction.[3]

Recently, our research interest has been in the application of hypervalent iodine compounds in organic synthesis. Our previous works show that diaryliodonium salts are excellent electrophilic arylating reagents[4] and notably ionic liquids can accelerate their arylation.[5] As part of a program to investigate the range of organic reactions possible in ionic liquids, coupled with the high reactivity of diaryliodonium salts, we examined the reaction of benzothiazole-2-thiol with diaryliodonium salts in the ionic liquid 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4), which might provide a novel method for the synthesis of 2-arylthiobenzothiazoles (Scheme 1).

We found that the reaction of benzothiazole-2-thiol **1** with diaryliodonium salts **2** in [bmim]BF_4 occurred smoothly at 60°C and was completed within 1–2h to give the desired 2-arylthiobenzothiazoles **3** in good yields. The results are summarised in Table 1. All products were characterised by m.p., IR, ^{1}H NMR, or MS-spectra, which were consistent with the literature data.



1 **2** **3**

R = H, Cl, NO_2 X = Cl, Br, I

Scheme 1

As can be seen in Table 1, the present method shows an efficient entry from S-arylated benzothiazole-2-thiol, allowing the preparation of 2-arylthiobenzothiazoles bearing various substituents such as the methyl, methoxy, bromo, chloro and nitro group on the phenyl ring. The ionic liquid [bmim]BF_4 can truly be compared with classical molecular solvents, with the advantage of rate acceleration and increase of yield. For example, the preparation of 2-phenylthiobenzothiazole (**3a**) was successful in [bmim]BF_4 for only 2 hours and gave a higher yield (Entry 1), but the same reaction run in the classical molecular solvents, such as THF, DMF or acetonitrile, gave lower yields when accomplished within 6–10 h (Entries 4, 5 and 6). On the other hand, the ionic liquid ([bmim]BF_4) could be typically recovered after extraction of the products and reused for further reactions with no appreciable decrease in yield (Entries 2 and 8). We also found the related ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate [bmim]PF_6 seemed to be favourable at 80°C for S-arylation of benzothiazole-2-thiol with diphenyliodonium chloride (Entry 3).

Table 1 S-Arylation of benzothiazole-2-thiol with diaryliodonium salts in ionic liquids and organic solvents.

Entry	R	Ar	X	medium	Product	Yield[a]/%
1	H	Ph	Cl	[bmim]BF_4	**3a**	85
2	H	Ph	Cl	[bmim]BF_4	**3a**	84[b]
3	H	Ph	Cl	[bmim]PF_6	**3a**	83[c]
4	H	Ph	Cl	THF	**3a**	61[d]
5	H	Ph	Cl	DMF	**3a**	49[d]
6	H	Ph	Cl	acetonitrile	**3a**	53[d]
7	H	*p*-Tol	Cl	[bmim]BF_4	**3b**	86
8	H	*p*-Tol	Cl	[bmim]BF_4	**3b**	84[b]
9	H	*p*-$MeOC_6H_4$	Cl	[bmim]BF_4	**3c**	79
10	H	*p*-$MeOC_6H_4$	Br	[bmim]BF_4	**3c**	70
11	H	*p*-$MeOC_6H_4$	I	[bmim]BF_4	**3c**	58
12	H	*p*-ClC_6H_4	Cl	[bmim]BF_4	**3d**	92
13	H	*p*-BrC_6H_4	Cl	[bmim]BF_4	**3e**	89
14	H	*m*-$NO_2C_6H_4$	Cl	[bmim]BF_4	**3f**	87
15	5-Cl	Ph	Cl	[bmim]BF_4	**3g**	85
16	6-NO_2	Ph	Cl	[bmim]BF_4	**3h**	81

[a]Isolated yield based on diaryliodonium salts. [b]Using recovered [bmim]BF_4. [c]Reaction was run at 80°C for 2h. [d]Reactions were run at 60°C for 6–10h.

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Finally, the reactivity of halogen counterions in the 4,4'-dimethoxy- diphenyliodonium salt were tested (Entries 9, 10 and 11). We found that the more electron withdrawing the anion, the better the yield in the reaction, which is in accordance with the literature.[6]

Much attention has been focused on the synthesis of 2-substituted thiobenzothiazoles, which constitute a biologically active and pharmaceutically important class of compounds.[7] These compounds are of interest as fungicides.[8] The usual synthesis of 2-arylthiobenzothiazoles involves the reaction of 2-halogeno-benzothiazoles with thiophenols, or better their alkali metal salts.[7e, 9] The nucleophilic substitution reaction between aryl halides and benzothiazole-2-thiol anions represents an alternative route,[7d,10] but this methodology is only suitable to the substrates activated by strong electron-withdrawing substituents such as the nitro group on haloarenes. 2-Arylthiobenzothiazoles are also available by the reaction of benzothiazole-2-thiol with aryldiazonium salts in the presence of alkali,[11] but this method gave a low yield (10–32 %) of products. To the best of our knowledge, there is no practical synthetic route available for the preparation of different 2-arylthiobenzothiazoles by direct S-arylation of benzothiazole-2-thiol.[12] The present work represents the first useful example of S-arylation of benzothiazole-2-thiol for the synthesis of 2-arylthiobenzothiazoles. It has some distinct advantages including simplicity of the methodology, the ease of product isolation, good yields of products, environmentally more benign, and potential for recycling of ionic liquid.

Experimental

^{1}H NMR spectra were recorded on Avance-400 spectrometer using $CDCl_3$ as the solvent with TMS as an internal standard. IR spectra were determined on PE-683 Infrared spectrophotometer with KBr pallet. Mass spectra were measured on a HP-5989B mass spectrometer. Melting points were not corrected.

General procedure for the preparation of 2-arylthiobenzothiazoles: To a stirred ionic liquid [bmim]BF_4 (4 ml) was added benzothiazole-2-thiol **1** (1.2 mmol), and warmed at 60°C until the whole was dissolved. Then diaryliodonium salt **2** (1 mmol) was added. The mixture was stirred at 60°C for 1–2h. The resulting solution was cooled to room temperature and extracted with diethyl ether (10 ml × 3). The combined ether extracts were concentrated *in vacuo* to give a residue, which was chromatographed on silica gel plate using cyclohexane/ethyl acetate (4:1) as the developer to provide pure products **3**. After extracting to isolate the product, the rest of the viscous ionic liquid was further washed with ether and dried at 80°C under reduced pressure to retain its activity in subsequent runs.

Physical and spectroscopic data

2-(Phenyl)thiobenzothiazole **3a**[9d]: oil; ^{1}H NMR δ_H 7.92–8.10 (m, 2H), 7.25–7.78 (m, 7H); IR ν_{max}/cm^{-1} 3100, 1635, 1458, 1432, 1313, 1268, 993, 758, 693.

2-(4-Methylphenyl)thiobenzothiazole **3b**: m.p.70–71°C (lit[9c] 71–72°C); ^{1}H NMR δ_H 7.86 (m, 2H), 7.53 (d, 2H, *J*=8.1 Hz), 7.43–7.32 (m, 2H), 7.15 (d, 2H, *J*=8.1 Hz), 2.32 (s, 3H); IR ν_{max}/cm^{-1} 3042, 1620, 1450, 1420, 1020, 1010, 820, 760, 755.

2-(4-Methoxyphenyl)thiobenzothiazole **3c**[11]: m.p.58–60 °C; ^{1}H NMR δ_H 7.88–7.80 (m, 2H), 7.64 (d, 2H, *J*=8.6 Hz), 7.43–7.33 (m, 2H), 6.84 (d, 2H, *J*=8.8 Hz), 3.78 (s, 3H); IR ν_{max}/cm^{-1} 2925, 1632, 1580, 1493, 1455, 1427, 1291, 1250, 1172, 1027, 1003, 830, 759, 530; MS *m/z* 274(31.22), 273 (M^+, 100), 272(80.47), 258(20.97), 96(22.60), 95(22.69), 69(27.90), 63(29.88).

2-(4-Chlorophenyl)thiobenzothiazole **3d**[11]: m.p.54–56 °C; ^{1}H NMR δ_H 7.92–7.90 (d, 2H), 7.71-7.67(m, 3H), 7.49–7.42(m, 3H); IR ν_{max}/cm^{-1} 3058, 2923, 1634, 1571, 1474, 1455, 1426, 1390, 1240, 1092, 1007, 819, 751, 725, 497; MS *m/z* 279(25.42), 278(49.62), 277(62.29), 276 (M^+, 100), 108(31.76), 75(13.29), 69(19.11), 63(15.68).

2-(4-Bromophenyl)thiobenzothiazole **3e**[11]: m.p.98–101 °C; ^{1}H NMR δ_H 8.12–8.09 (m, 3H), 7.70–7.65 (m, 3H), 7.26 (s, 2H), IR ν_{max}/cm^{-1} 3102, 2924, 1632, 1518, 1357, 1106, 1067, 853, 840, 738; MS *m/z* 323(14.32), 322(M^+, 27.36), 321(14.36), 320(23.60), 117(15.74), 97(28.57), 85(38.21), 83(30.73), 71(57.65), 69(47.55), 57(88.43), 55(51.22), 43(76.43), 41(42.05)

2-(3-Nitrophenyl))thiobenzothiazole **3f**: m.p.88–90 °C (lit[7e] 90.5–91 °C); ^{1}H NMR δ_H 8.80–8.69(s, 1H), 8.45–8.37(m, 2H), 7.72–7.60(m, 2H), 7.15–6.93(m, 3H); IR ν_{max}/cm^{-1} 3047, 1630, 1560, 1510, 1460, 1330, 1240, 1050, 895, 870, 784, 683.

5-Chloro-2-(Phenyl)thiobenzothiazole **3g**: m.p.87–89 °C (lit[12] 89–90 °C); ^{1}H NMR δ_H 8.40–8.21(m, 2H), 7.40–7.20(m, 2H), 7.18–7.07(m, 4H); IR ν_{max}/cm^{-1} 3029, 1632, 1590, 1540, 1425, 1300, 1245, 1052, 891, 736.

6-Nitro-2-(Phenyl)thiobenzothiazole **3h**: m.p.105–107 °C (lit[9b] 104 °C); ^{1}H NMR δ_H 8.54(d, 1H), 7.85(m, 1H), 7.78(m, 3H), 7.30–7.23(m, 3H); IR ν_{max}/cm^{-1} 3040, 1625, 1540, 1486, 1454, 1350, 1335, 1165, 743.

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